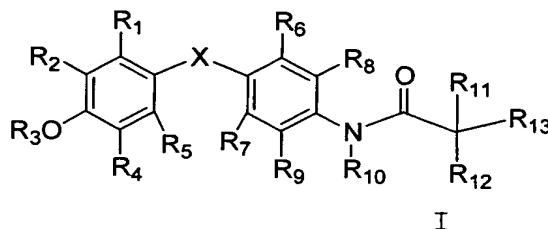


WHAT IS CLAIMED IS:

1. A compound of the formula I



Wherein:

X is selected from oxygen (-O-), selenium (-Se-), sulfur (-S-), sulfenyl (SO), sulfonyl (SO₂), carbonyl (-CO), methylene (-CH₂-) and -NH-;

R₁ is selected from hydrogen, halogen, CF₃ and C₁ to C₆ alkyl;

R₂ is selected from halogen, CF₃, C₁ to C₆ alkyl, C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, C₃ to C₇ cycloalkyl, C₄ to C₇ cycloalkenyl, aryl, heteroaryl, alkoxy, aryloxy, COR₁₄, CR₁₄(OR₁₀)R₁₅, heteroaryloxy, arylalkoxy, cycloalkoxy, N(R₁₄)COR₁₅, CO(NR₁₄R₁₅), N(R₁₄)SO₂R₁₆, SO₂(NR₁₄R₁₅), SR₁₆, SOR₁₆, SO₂R₁₆, and CH₂NR₁₄R₁₅;

R₃ is selected from hydrogen, alkyl, benzyl, aroyl and alkanoyl;

R₄ is halogen or alkyl;

R₅ is hydrogen, halogen or alkyl;

R₆ and R₇ are each independently selected from hydrogen, halogen, cyano, C₁ to C₄ alkyl and C₃ to C₆ cycloalkyl, where at least one of R₆ and R₇ is not hydrogen;

R₈ and R₉ are each independently selected from hydrogen, halogen, alkoxy, hydroxy(-OH), cyano, CF₃ and alkyl, where at least one of R₆ and R₇ is not hydrogen; provided that no more than one of R₆, R₇, R₈ and R₉ is hydrogen;

R₁₀ for each occurrence is independently selected from hydrogen or alkyl;

R₁₁ is CO₂R₁₄;

R₁₂ and R₁₃ are each independently selected from hydrogen, halogen and alkyl;

R₁₄ and R₁₅ for each occurrence are each independently selected from hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl; and

R₁₆ for each occurrence is independently selected from selected from alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl,

including all prodrugs, stereoisomers and pharmaceutically acceptable salts thereof.

2. The compound as defined in Claim 1 wherein X is oxygen.

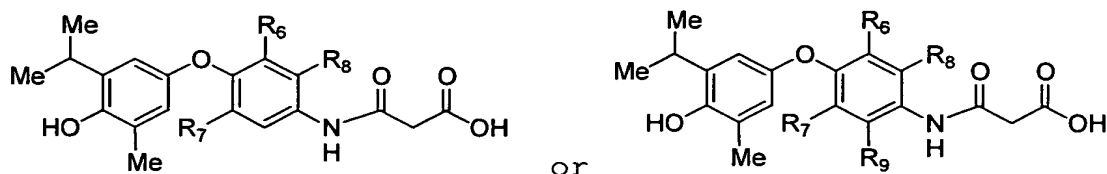
3. The compound as defined in Claim 2 wherein
R₁ is hydrogen;
R₂ is C₁ to C₆ alkyl or C₃ to C₇ cycloalkyl;
R₃ is hydrogen;
R₄ is halogen or C₁ to C₄ alkyl;
R₅ is hydrogen;
R₆ and R₇ are independently bromo, chloro or methyl;
R₈ is halogen or C₁ to C₄ alkyl;
R₉ is hydrogen or halogen;
R₁₀ is hydrogen;
R₁₁ is carboxyl;
R₁₂ is hydrogen; and
R₁₃ is hydrogen.

4. The compound as defined in Claim 3 wherein R₂ is isopropyl.

5. The compound as defined in Claim 2 wherein
 R_1 is hydrogen;
 R_2 is isopropyl;
 R_3 is hydrogen;
5 R_4 is C_1 to C_4 alkyl;
 R_5 is hydrogen;
 R_6 and R_7 are independently bromo, chloro or methyl;
 R_8 is halogen or methyl;
 R_9 is hydrogen or chloro;
10 R_{10} is hydrogen;
 R_{11} is carboxyl;
 R_{12} is hydrogen; and
 R_{13} is hydrogen.

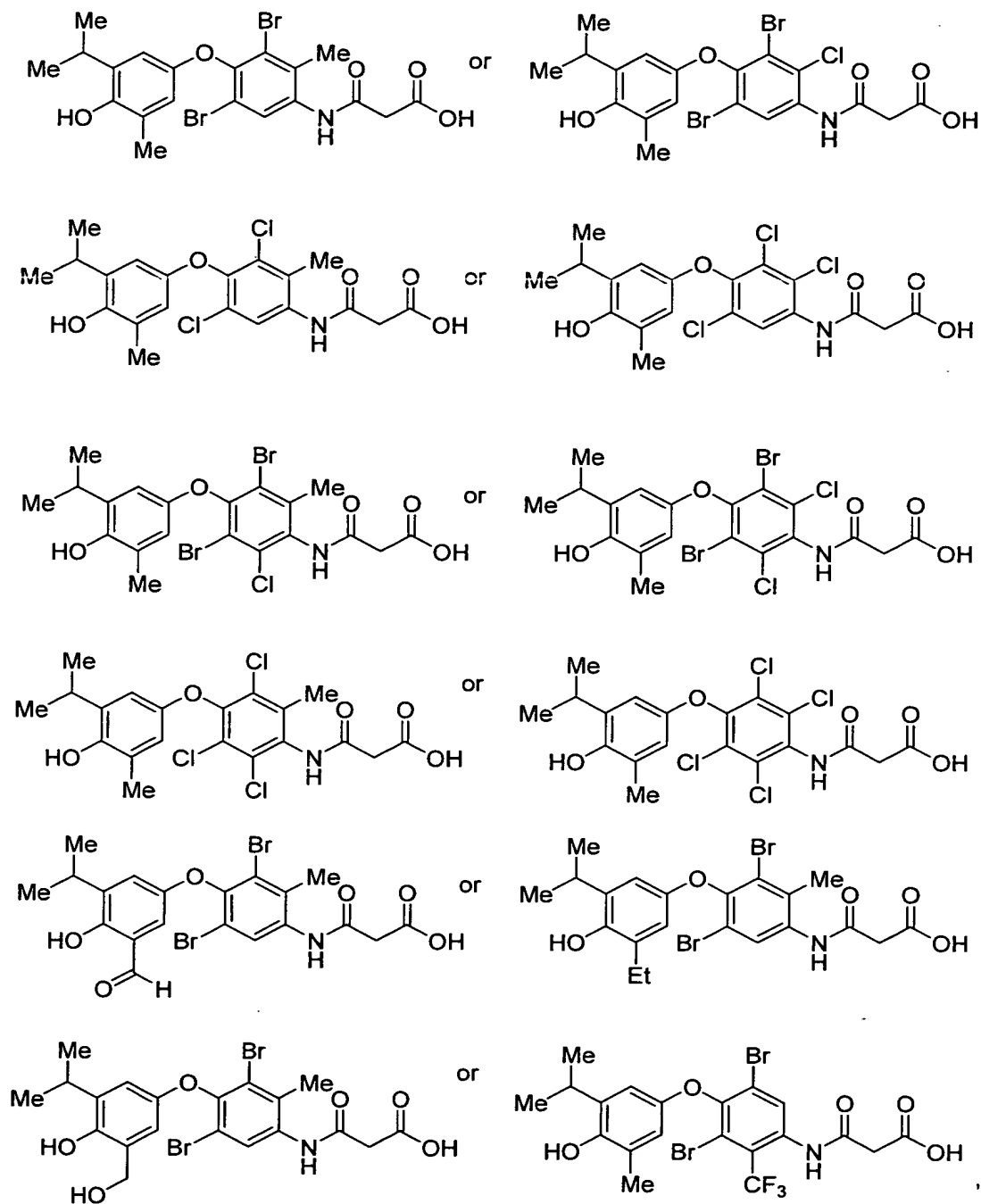
15 6. The compound as defined in Claim 2 wherein
 R_1 is hydrogen;
 R_2 is isopropyl;
 R_3 is hydrogen;
 R_4 is methyl;
20 R_5 is hydrogen;
 R_6 and R_7 are independently bromo or chloro;
 R_8 is chloro or methyl;
 R_9 is hydrogen;
 R_{10} is hydrogen;
25 R_{11} is carboxyl;
 R_{12} is hydrogen; and
 R_{13} is hydrogen.

30 7. The compound as defined in Claim 1 having the structure



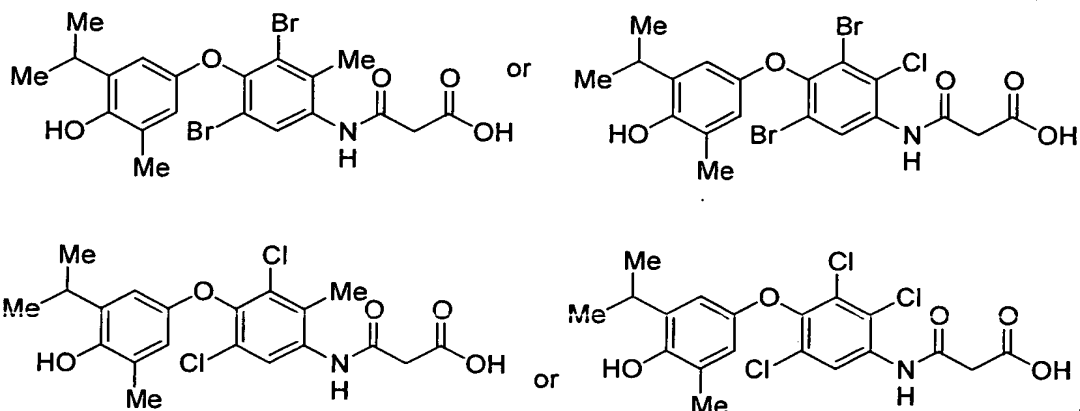
or an alkyl ester thereof.

8. The compound as defined in Claim 1 having the structure



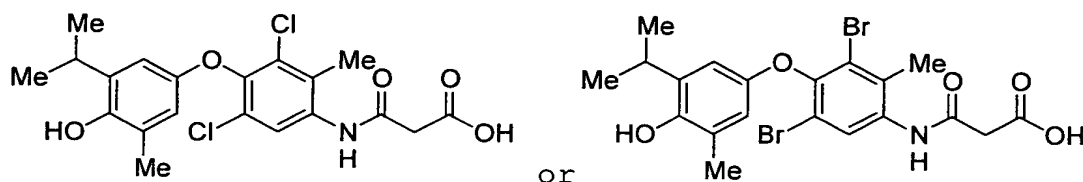
5 or an alkyl ester thereof.

9. The compound as defined in Claim 1 having the structure



5

10. The compound as defined in Claim 1 having the structure



10

11. A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

15

12. The pharmaceutical composition of claim 11 further comprising at least one additional therapeutic agent selected from other compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents, appetite suppressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

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13. The pharmaceutical composition of claim 12 wherein said additional therapeutic agent is an antidiabetic agent selected from a biguanide, a glucosidase inhibitor, a meglitinide, a sulfonylurea, a thiazolidinedione, a PPAR-alpha agonist, a PPAR-gamma agonist, a PPAR alpha/gamma dual agonist, an SGLT2 inhibitor, a glycogen phosphorylase inhibitor, an aP2 inhibitor, a glucagon-like peptide-1 (GLP-1), a dipeptidyl peptidase IV inhibitor and insulin.

10

14. The pharmaceutical composition of claim 12 wherein said additional therapeutic agent is an antidiabetic agent selected from metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, troglitazone, pioglitazone, englitazone, darglitazone, rosiglitazone and insulin.

15. The pharmaceutical composition of claim 12 wherein said additional therapeutic agent is an anti-obesity agent selected from an aP2 inhibitor, a PPAR gamma antagonist, a PPAR delta agonist, a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin reuptake inhibitor, a cannabinoid-1 receptor antagonist and an anorectic agent.

16. The pharmaceutical composition of claim 12 wherein said additional therapeutic agent is a hypolipidemic agent selected from thiazolidinedione, an MTP inhibitor, a squalene synthetase inhibitor, an HMG CoA reductase inhibitor, a fibric acid derivative, an ACAT inhibitor, a cholesterol absorption inhibitor, an ileal Na⁺/bile cotransporter inhibitor, a bile acid sequestrant and a nicotinic acid or a derivative thereof.

35

17. A method for preventing, inhibiting or treating a disease associated with metabolic dysfunction, or which is dependent on the expression of a T₃ regulated gene, which comprises administering to a mammalian patient in
5 need of treatment a therapeutically effective amount of a compound as defined in claim 1.

18. A method for treating or delaying the progression or onset of obesity, hypercholesterolemia,
10 atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or
15 a skin disorder or disease, which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

20 19. The method according to claim 18 wherein the skin disorder or disease is dermal atrophy, post surgical bruising caused by laser resurfacing, keloids, stria, cellulite, roughened skin, actinic skin damage, lichen planus, ichthyosis, acne, psoriasis, Dernier's disease,
25 eczema, atopic dermatitis, chloracne, pityriasis or skin scarring.

20. The method according to claim 18 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from other
5 compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents,
10 appetite suppressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

21. A method of treating or delaying the progression
15 or onset of a skin disorder or disease which comprises administering to a mammalian patient a therapeutically effective amount of a compound as defined in claim 1 in combination with a retinoid or a vitamin D analog.

20 22. A method for treating or delaying the progression or onset of obesity which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

25 23. A method according to claim 22 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from an anti-
30 obesity agent or an appetite suppressant.

24. A method according to claim 23 wherein said anti-obesity agent is selected from α 2 inhibitors, PPAR gamma antagonists, PPAR delta agonists, beta 3 adrenergic
35 agonists, lipase inhibitors, serotonin (and dopamine) reuptake inhibitors, cannabinoid-1 receptor antagonists, other thyroid receptor agents and anorectic agents.

25. A pharmaceutical composition which functions as a selective agonist of the thyroid hormone receptor comprising a compound as defined in claim 1.

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